

# Glomerulonephritis in Malignancy

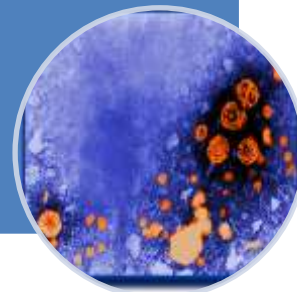
*Mostafa Abdel\_Salam Mohamed, MD*  
*MUH*

Paraneoplastic glomerulonephritis are glomerular lesions that are not directly related to tumor burden, invasion, or metastasis, but rather are induced by products from tumor cells.

# Why are Dialysis Patients at Risk for Infection?

- the first series of paraneoplastic glomerulonephritis was published over 40 years ago by lee et al.
- solid tumor-associated membranous nephropathy
- Hodgkin lymphoma-associated minimal change disease (mCD)

‘classic’  
paraneoplastic  
glomerulonephritides



Lee, J. C., Yamauchi, H. & Hopper, J. Jr. The association of cancer and the nephrotic syndrome. Ann. Intern. Med. 64, 41–51 (1966).

focal segmental glomerulosclerosis  
membrano proliferative glomerulonephritis,  
IGA nephropathy  
rapidly progressive glomerulonephritis

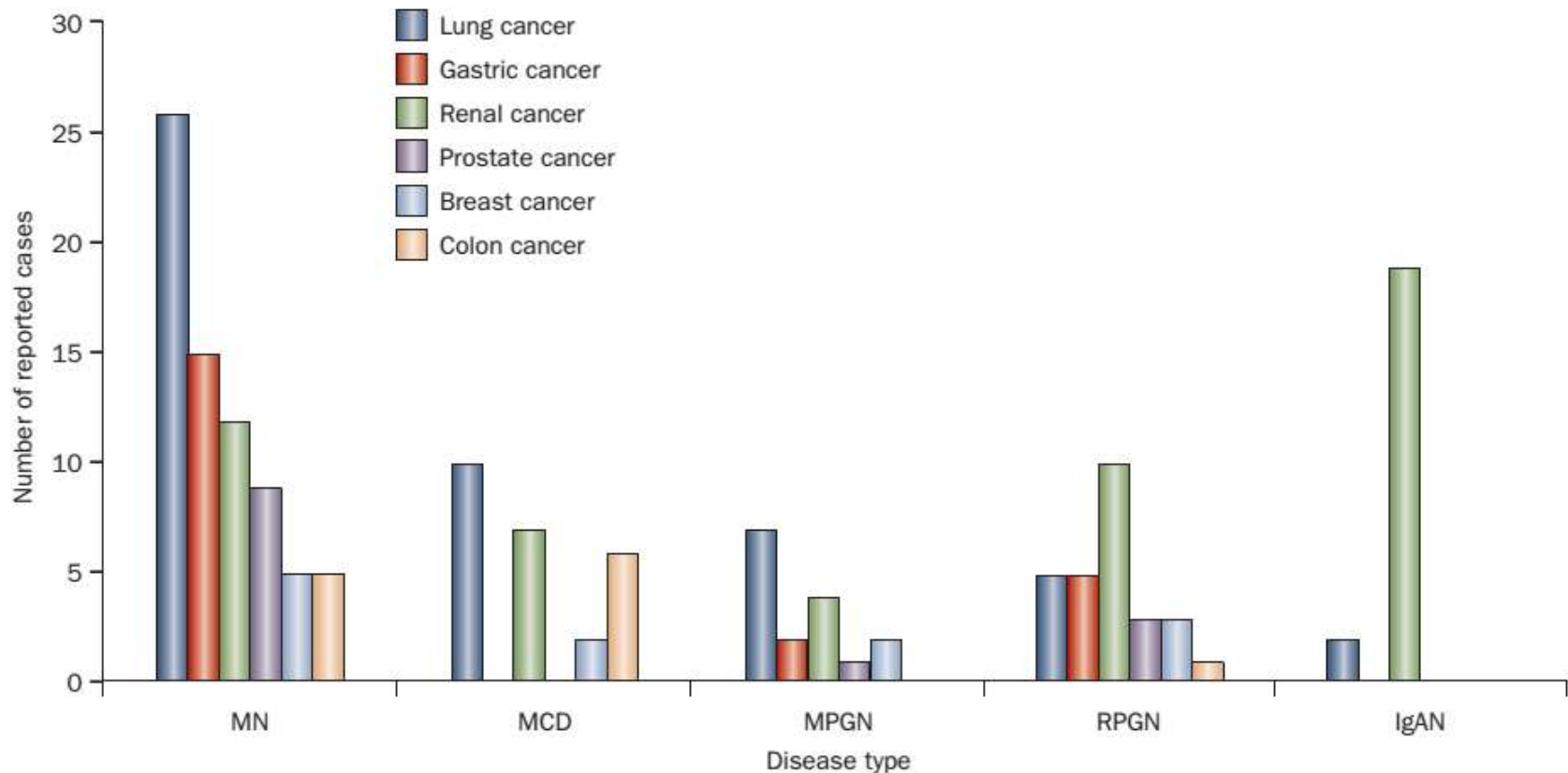
# Consider

glomerulonephritis occurs in the presence of malignancy

remits after ablation of the malignancy

recurs in association with the recurrence of malignancy.

# Solid Tumors



Mimura, i., Tojo, A., Kinugasa, S., Uozaki, H. & Fujita, T. Renal cell carcinoma in association with igA nephropathy in the elderly. *Am. J. Med. Sci.* 338, 431–432 (2009)

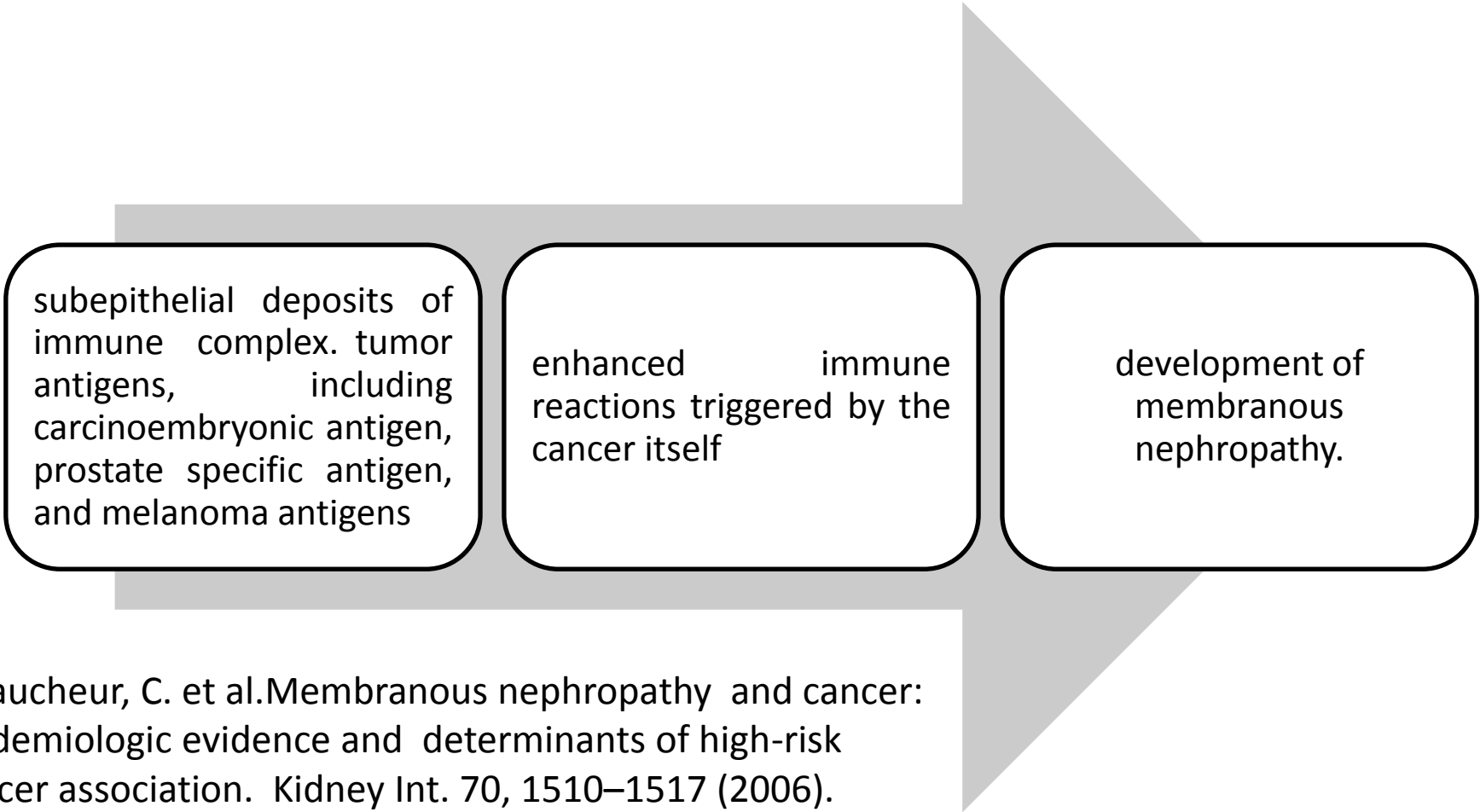
Bacchetta, J., Juillard, L., Cochat, P. & Droz, J. P. Paraneoplastic glomerular diseases and malignancies. *Crit. Rev. Oncol. Hematol.* 70, 39–58 (2009).

# Membranous Nephropathy

male

nephrotic syndrome

Active cancer (lung and prostate)



subepithelial deposits of immune complex. tumor antigens, including carcinoembryonic antigen, prostate specific antigen, and melanoma antigens

enhanced immune reactions triggered by the cancer itself

development of membranous nephropathy.

Lefaucheur, C. et al. Membranous nephropathy and cancer: Epidemiologic evidence and determinants of high-risk cancer association. *Kidney Int.* 70, 1510–1517 (2006).



increased number of inflammatory cells in glomeruli, igG1 and igG2 subtypes are markedly more prominent in the kidneys of patients with paraneoplastic membranous nephropathy than in those with idiopathic membranous nephropathy, whereas levels of igG4 are no different.

Ohtani, H. et al. Distribution of glomerular igG subclass deposits in malignancy-associated membranous nephropathy. Nephrol. Dial. Transplant. 19, 574–579 (2004).

- In paraneoplastic membranous nephropathy, both tH1 and tH2 cytokines may be activated by tumor antigens or other stimulants, resulting in the unique pattern of igG subtype and increased numbers of inflammatory cells.

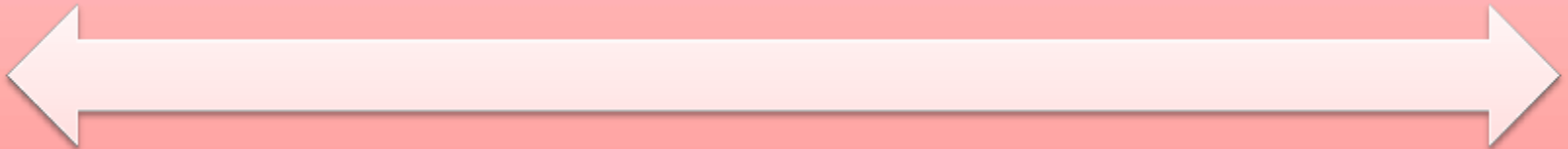
# Minimal Change Disease

MCD has been reported in association with lung, colon, and renal cancers

ablation of the tumor frequently results in remission of MCD



vascular endothelial growth factor  
increase glomerular permeability.



Taniguchi, K. et al. Rectal cancer with paraneoplastic nephropathy: association of vascular endothelial growth factor. Dig. Surg. 21, 455–457 (2004).

the role of veGF in the pathogenesis of MCD and FsGs further supported by the findings that overexpression of veGF in podocytes induces collapsing FsGsin experimental animal models and that serum veGF levels are elevated in children with nephrotic syndrome.



# Membranoproliferative Glomerulonephritis

lung, renal and gastric cancers

combination of tumor antigen formation and the inability of the host to effectively clear antigens.



# Rapidly Progressive Glomerulonephritis

renal cell carcinoma, gastric, and lung cancers

the pathogenetic mechanisms by which neoplasms lead to the development of ANCA-associated vasculitis and rPGN largely unknown




# IGA Nephropathy

solid tumors of the respiratory tract, buccal mucosa and nasopharynx

the paraneoplastic nature of IGA nephropathy is supported by the finding that IGA nephropathy resolved after tumor removal and evidence of IGA staining within the renal cell carcinoma.



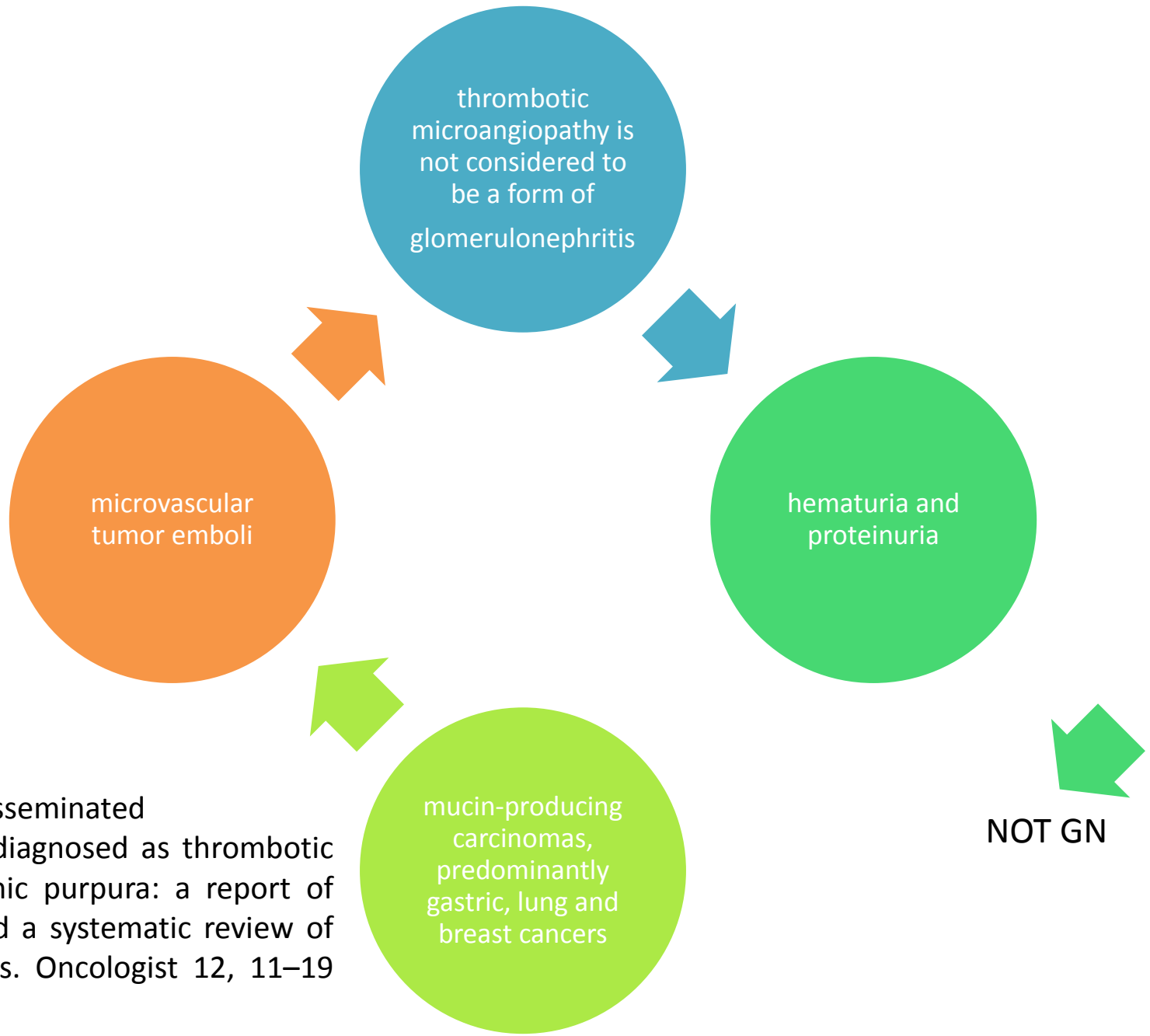


Henoch–schönlein purpura (HsP)  
a systemic vasculitis that occurs in  
association with IGA nephropathy has also  
been reported in association with solid  
tumors, most commonly lung cancers



# Thrombotic Microangiopathy

multisystemic disorder that leads to thrombocytopenia, microangiopathic hemolytic anemia and ischemic manifestations owing to platelet agglutination. Damage to the central nervous system and kidney can also manifest



Francis et al., Disseminated malignancy misdiagnosed as thrombotic thrombocytopenic purpura: a report of 10 patients and a systematic review of published cases. *Oncologist* 12, 11–19 (2007)

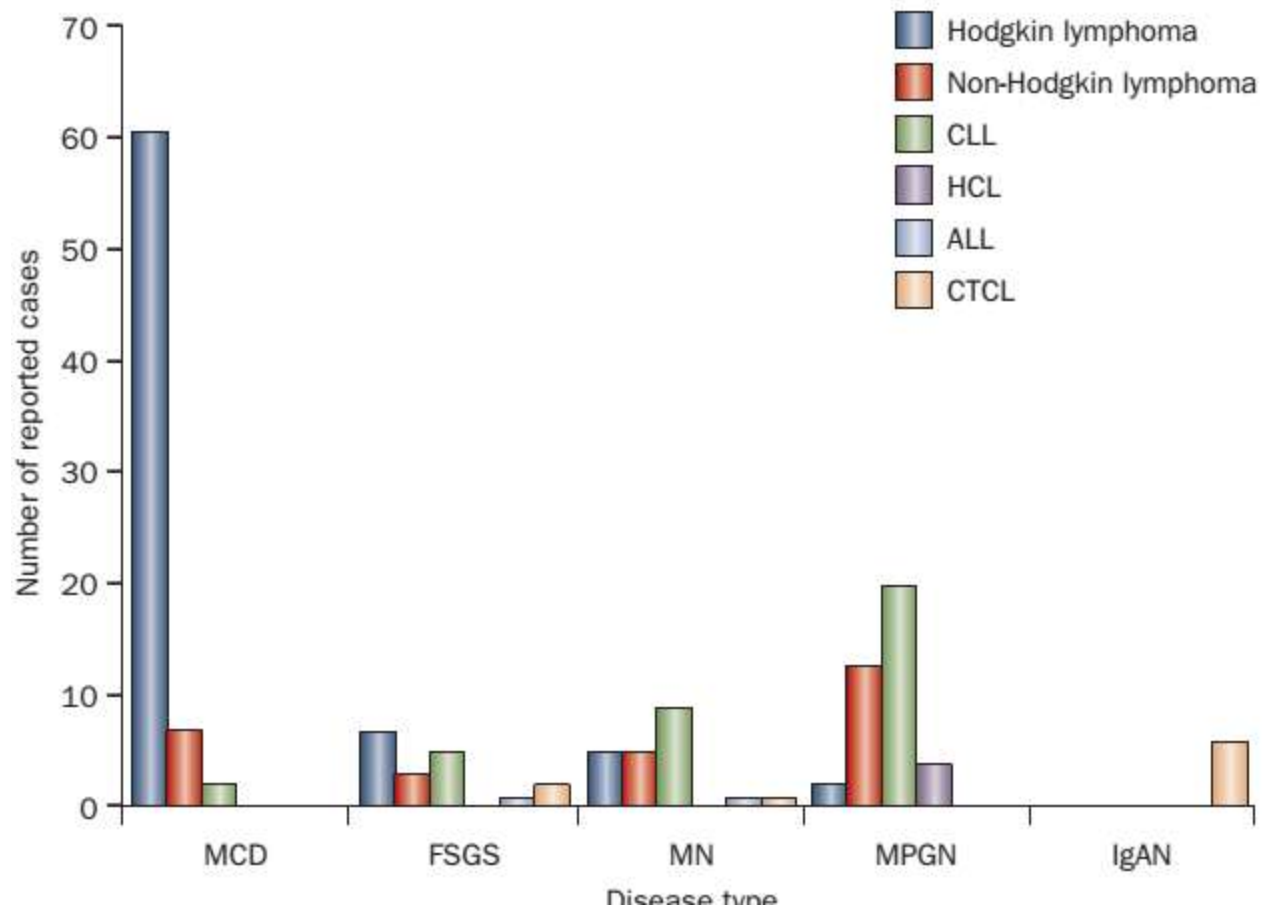
Patients with cancer associated  
thrombotic microangiopathy do  
not have severely impaired  
ADAMTS-13 activity and respond  
poorly to plasma exchange therapy  
poor prognosis

# Hematological Malignancies

Lymphoid,  
Myeloid  
thymus malignancies

# lymphoid Malignancies

Paraneoplastic glomerulonephritides are well known to occur in association with chronic lymphoid neoplasms, but rarely occur in patients with acute lymphocytic leukemia



# MCD and FSGS

- MCD occurs in about 1% of patients with Hodgkin lymphoma and the occurrence of FSGS is about one tenth that of MCD
- A poor response of MCD to steroid or cyclosporin therapy therefore seems to be indicative of occult Hodgkin lymphoma

Mallouk, A., Pham, P. T. & Pham, P. C. Concurrent FSGS and Hodgkin's lymphoma: case report and literature review on the link between nephrotic glomerulopathies and hematological malignancies. Clin. Exp. Nephrol. 10, 284–289 (2006)





Increased cytokine levels, particularly levels of tH2 cytokines

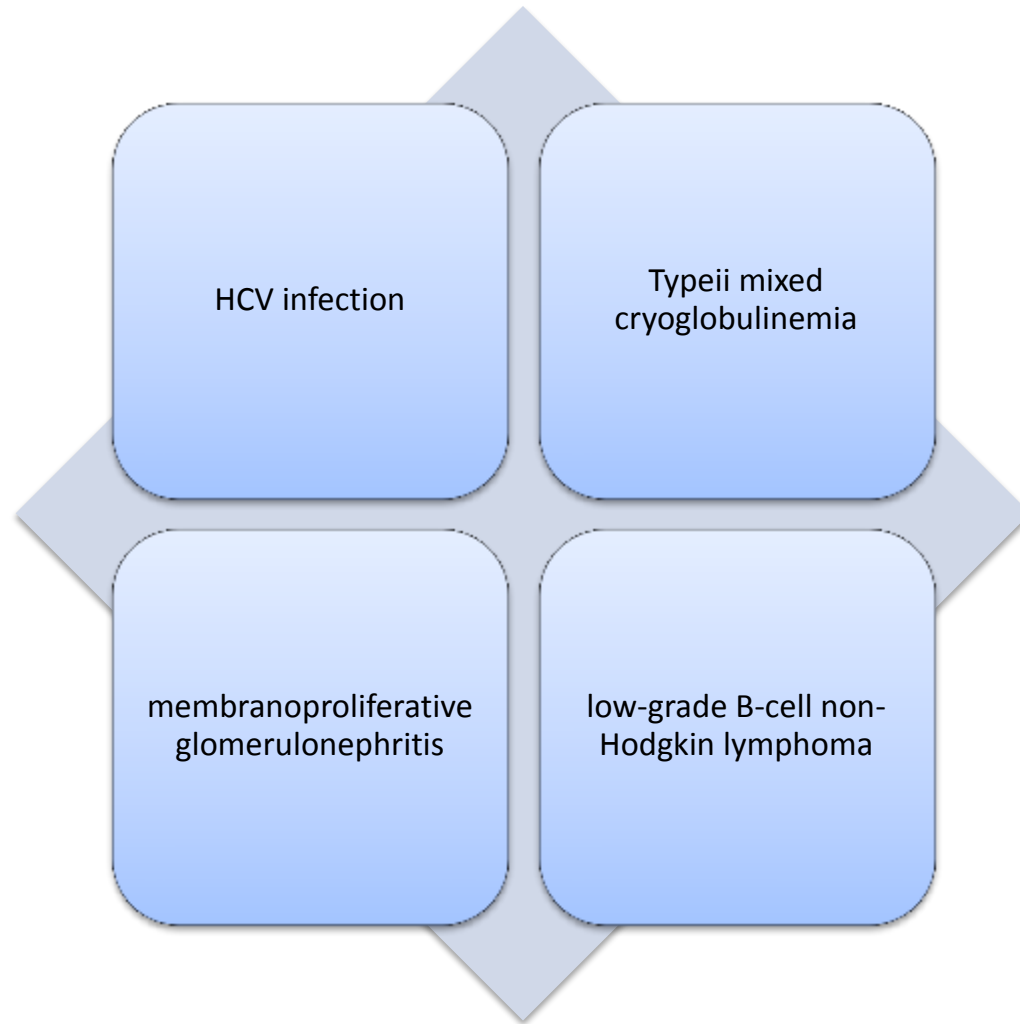
il-13, a tH2-type cytokine, and its receptor are constitutively expressed in reed–sternberg cells in patients with Hodgkin lymphoma.

# Membranoproliferative Glomerulonephritis

the incidence of nephrotic syndrome in patients with chronic lymphocytic leukemia is less than 1%, with membranoproliferative glomerulonephritis being the most common pathology

monoclonal immunoglobulin

mixed cryoglobulinemia, mainly comprising types i and ii,



# Membranous Nephropathy

monoclonal proteins produced by B cells may be involved in the pathogenesis of para neoplastic membranous nephropathy





# IGA nephropathy

tH2 polarization has been observed in patients with cutaneous t-cell lymphoma



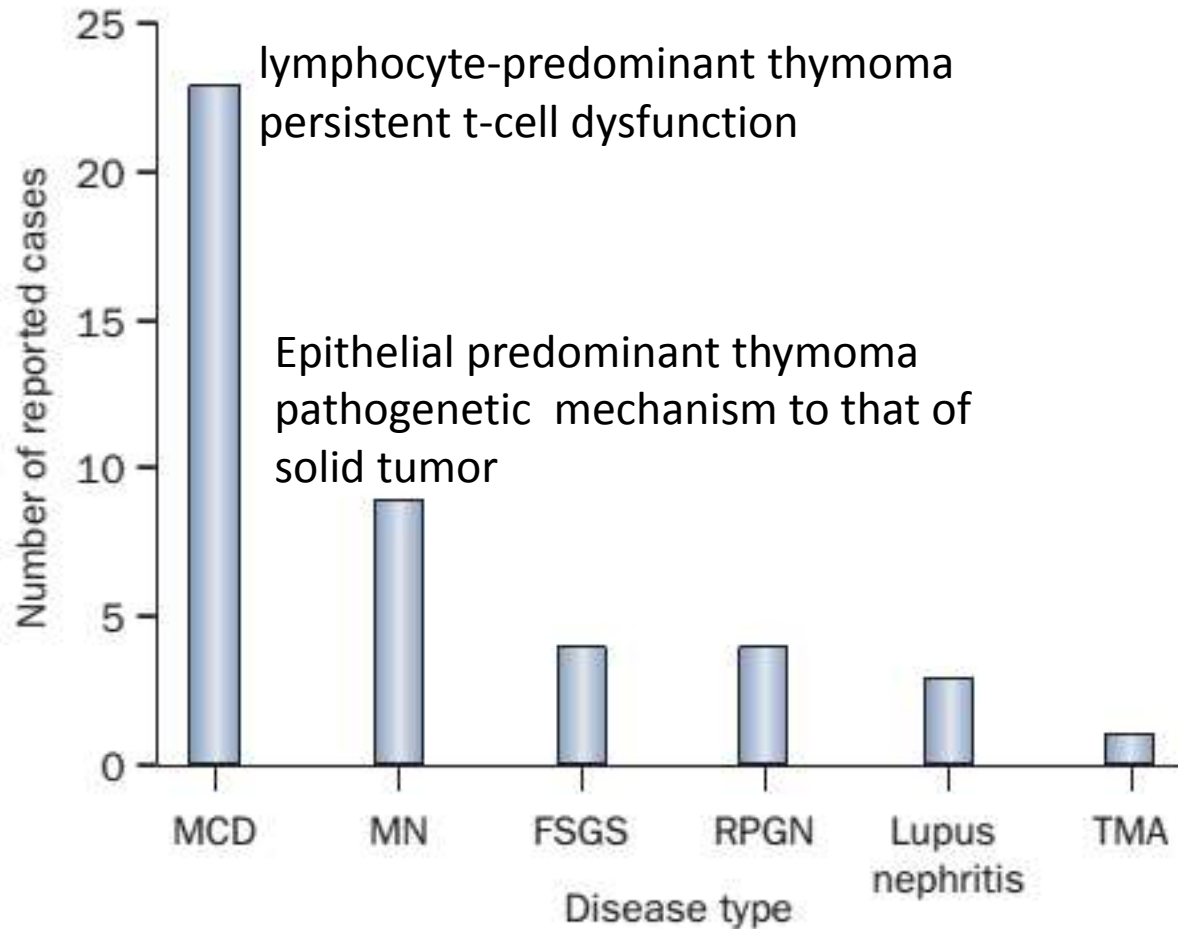
# Myeloid Malignancies

paraneoplastic glomerulonephritides have been reported infrequently in patients with myeloid neoplasms  
FSGS/MCD/MPG

Table 1   The 2008 WHO classification of chronic myeloid neoplasms		
Category	Characteristics	Diseases
Myeloproliferative neoplasms	Effective maturation of RBCs, WBCs, and platelets	Chronic myelogenous leukemia, polycythemia vera, essential thrombocythemia, primary myelofibrosis, chronic neutrophilic leukemia, chronic eosinophilic leukemia, mastocytosis, unclassifiable myeloproliferative neoplasms
Myelodysplastic syndrome	Ineffective maturation of RBCs, WBCs or platelets with dysplastic features	Refractory cytopenia with unilineage dysplasia, refractory anemia with ring sideroblasts, refractory cytopenia with multilineage dysplasia, refractory anemia with excess sideroblasts, myelodysplastic syndrome with isolated deletion of chromosome 5q, unclassifiable myelodysplastic syndrome, refractory cytopenia of childhood
Myelodysplastic–myeloproliferative disorders	Hybrid dysplastic and proliferative features	Chronic myelomonocytic leukemia, juvenile myelomonocytic leukemia, atypical chronic myeloid leukemia, unclassifiable myelodysplastic–myeloproliferative neoplasms
Abbreviations: RBC, red blood cell; WBC, white blood cell.		



# Thymoma



the prevalence of paraneoplastic glomerular diseases in patients with thymoma is about 2%, higher than that for Hodgkin lymphoma

# Questions??

